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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,283	01/09/2001	Yuti Chernajovsky	0623.1000000/LLB/PAJ	5963

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EXAMINER
ANDRES, JANET L

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/10/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,283	CHERNAJOVSKY ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1646	

-- Th MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,23 and 24* is/are pending in the application.

4a) Of the above claim(s) *6-17,19-21,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 18* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 13 is acknowledged. Claims 1-21, 23, and 24 are pending in this application. Claims 6-17, 19-21, 23, and 24 are withdrawn from consideration as being drawn to a non-elected invention. The restriction requirement of Paper No. 12 is made FINAL.

Specification

2. The disclosure is objected to because of the following informalities: There are sequences on pages 24-27 and in figures 1-4 that lack sequence identifiers.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-5 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 91/08291 (Levinson et al.). As written, these claims encompass a method of conferring latency on TGF-β using a latency-associated peptide. Latent forms of TGF-β and proteins that confer latency on the mature form are taught on p. 4, lines 6-14, and p. 5, lines 1, 2, and 10-37. Cleavage sites are taught in Figure 1. WO 91/08291 further teaches combination of the latency associated peptide with mature TGF-β for therapeutic purposes (p. 6, lines 19 and 20).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/08291 in view of U.S. patent 5908626 (Chang et al., 1999).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. WO 91/08291 teaches as set forth above, and further teaches that latency associated peptide can be administered with TGF-β to form a complex that can be activated *in vivo* (abstract, p. 7, lines 9-15 and 32-37, p 8, lines 1 and 2). WO 91/08291 fails to teach association of latency associated peptide with other factors. The '626 patent teaches fusion of interferon with an Fc fragment or with gelatin in order to prolong the half-life of the interferon (column 1, lines 33-36 and 55-67). The '626 patent also teaches that cytokines generally have short half-lives and that this undesirable (column 2, lines 28-38). It would have been obvious to one of ordinary skill in the art, on reading the teachings of WO 91/08291 and the '626 patent, to

substitute a cleavable latency associated peptide for the Fc protein of the '626 patent, thus generating a fusion protein comprising latency associated peptide, a cleavage site, and cytokine. One of ordinary skill would have been motivated to do so because WO 91/08921 teaches that a cleavable complex of latency associated peptide and the cytokine TGF-β is useful for the administration of TGF-β, and the '626 patent teaches that stabilization of other cytokines is desirable and can be achieved by fusion with the appropriate molecule.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fusion of a latency associated peptide with cytokines, does not reasonably provide enablement for fusion of such peptides with all pharmaceutically active agents, nor for the treatment of all diseases with all such agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

These claims are broadly drawn to encompass non-protein agents and proteins unrelated in structure and function to growth factors and cytokines. Latency associated peptides function by associating with the mature form of TGF-β. Applicant has shown effects with another cytokine, IFN. There is no guidance to indicate that LAP could form complexes with either non-protein agents or proteins with structures very different from cytokines and growth factors. One skill in the art would thus not predict, based on the teachings of the prior art and Applicant's disclosure, that LAP could be used with all agents as broadly claimed, nor could one of skill determine what other agents potentially within the scope of the claims could be used. There are no teachings to indicate how one of skill might determine which other agents, if any, could associate with LAP and be stabilized by this association.

Claim 18 is drawn to a method of treatment and is not limited to any disease or type of disease. It thus encompasses all diseases, including those for which no treatment is known in the art. What is shown is the treatment of inflammatory disease by interferons. One of skill in the art would not predict, based on Applicant's disclosure of one condition, that all diseases, including diseases unrelated to inflammation and diseases not known to be treatable, could be treated by the claimed method.

Thus, without further guidance, it would require undue experimentation for the skilled artisan to make and use Applicant's invention as broadly claimed.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are drawn to methods comprising "associating" a fusion protein with an agent. The specification fails to define "associating"; one of skill would not be able to determine whether the agent was part of the fusion protein, or how it was otherwise associated. Thus one of ordinary skill would not be able to determine what the method was intended to produce, nor what would be administered in the method of claim 18.

Claim Objections

Claim 18 is objected to as depending from a non-elected claim.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
September 3, 2002

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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